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Case report

Sweet's syndrome with pulmonary involvement: Case report and literature review☆

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ABSTRACT

A 74 year old female presented with fever, associated with papules and plaque in her upper and lower extremities. Exams revealed blood leukocytosis and a positive urine culture. Antibiotic therapy was initiated with no clinical response. After 1 week, chest X-ray showed right upper lobe alveolar infiltrate. A skin biopsy of the lesion showed infiltration by neutrophils, consistent with Sweet's Syndrome. Patient's condition progressively worsened, requiring oxygentherapy. Bronchoscopy and bronchoalveolar lavage were normal, transbronchial biopsies suggested lung involvement of Sweet 's syndrome. Antibiotic therapy was stopped. Corticosteroid were started. Therapy resulted in rapid clinical and radiological improvement.

1. Introduction

Sweet's Syndrome (SS) or acute febrile neutrophilic dermatosis is a systemic inflammatory disorder characterized by high fever, leukocytosis, and tender erythematous skin lesion. Histologically, dense dermal infiltrations of mature neutrophilic plaques with nuclear fragmentation and absences of signs of vasculitis are characteristic. Although recent reports suggest that vasculitis do not exclude SS.[1–3]

This syndrome typically occurs in middle – aged females. The etiology can be idiopathic (±70% of cases), parainflammatory (infection, autoimmune disorder and vaccination), paraneoplastic (hematopoietic disorders like myeloproliferative disorder, leukemia, etc).[1,4,5]

This disorder typically involves multiple organ system; pulmonary involvement in SS is quite rare. The classic pulmonary manifestations of SS described in the literature consist of bilateral infiltrates, pleural effusion and bronchiolitis obliterans – organizing pneumonia (BOOP).[4–11]

Systemic corticosteroid therapy is the treatment of choice for SS, achieving prompt improvement. Colchicine, indomethacin, cyclosporine and other immunosuppression therapies have been used for treatment.

We report the case of a female with myelodisplastic syndrome with SS associated with pulmonary manifestations. Skin and lung biopsies revealed neutrophilic infiltrates without vasculitic changes. Respiratory involvement responded to corticosteroid therapy. A search of the literature was carried out in the Medline and Lilacs Database, using the keywords: "Sweet Syndrome", alone and in conjuction with various terms such as "pulmonary inflammation", "lung". Further hand-searches were made based on the reference list of key papers. A total of 34 cases of SS with pulmonary involvement were found.

2. Case report

A 74 - year - old female with a history of ovarian cancer treated with chemotherapy and myelodysplastic syndrome diagnosed 5 months ago, was admitted at the hospital with a 2-month history of erythematous lesions at the lower extremities, associated with fever up to 38 °C. Physical examination, found an erythematous lesions at lower and upper extremities, moderately uplifted, 3–10 cm diameter, painful, associated to fever (39 °C). Blood exam showed leukocytosis and a urine culture was positive for *Escherichia coli*, antibiotic treatment was initiated with cefotaxime. After seven days receiving antibiotic therapy, no clinical response was observed. The patient developed progression of skin lesions and erythematous plaques, malaise, cough, dyspnea, persistent fever and chills. A chest X-ray revealed alveolar infiltrates at right upper lobe. Chest CT-scan was consistent with chest X-ray findings (Fig. 1).

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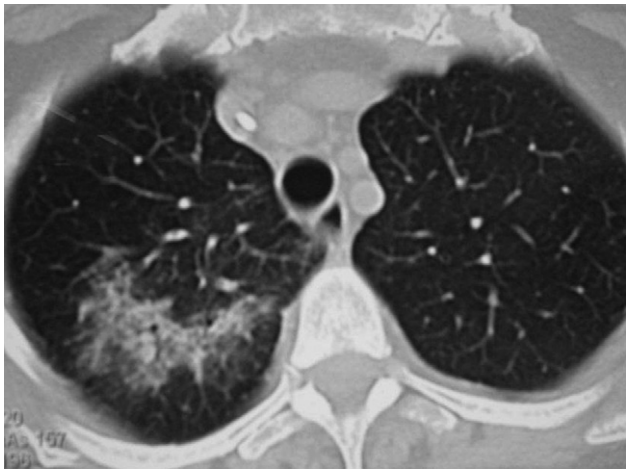

Fig. 1. Unilateral infiltrate on chest CT.

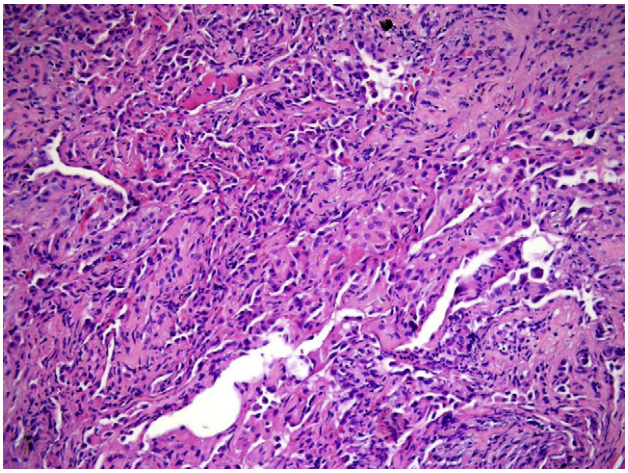

Fig. 3. Transbronchial biopsy showed neutrophils and edema.

Dermatological evaluation and a skin biopsy was performed and revealed edema and dense neutrophilic infiltrates in the dermis without vasculitis. No mucosal involvement was founded. The result was consistent with SS. (Fig. 2.)

Patient's condition progressively worsened, requiring oxygen-therapy. A videobronchoscopy with bronchoalveolar lavage (BAL) was performed, cytological and microbiological studies were negative. Antibiotic therapy was modified to imipenem, without any improvement. Amphotericin B administration was initiates as well.

Pulmonary signs did not improve on treatment with antifungal. A new chest-CT scan revealed increased alveolar infiltrates in the right upper lung with bilateral pleural effusion. A thoracocentesis was performed, consistent with a transudate.

A second videobronchoscopy with BAL and transbronchial biopsies were performed. Cytological study revealed a total cell count of 3.600 cell/ml, 72% neutrophils, 20% macrophages and 8% lymphocytes, new cultures were negative. Histopathological examination of the lung biopsy revealed extensive neutrophils infiltration with fibrin at the alveolar level, edema and focal acute and organizing pneumonia. (Fig. 3). This histological findings were similar to the one performed in the skin.

Antifungal therapy was stopped. The patient was treated with methylprednisolone (500 mg IV for 3 days) followed by oral prednisone. Steroid therapy produced a rapid improvement of cutaneous and pulmonary involvement. Patient had rapid clinical and radiographic resolution. After 2 weeks of therapy, erythematous plaques and skin lesions decreased. No recurrence was observed and chest CT scan showed a substantial improvement.

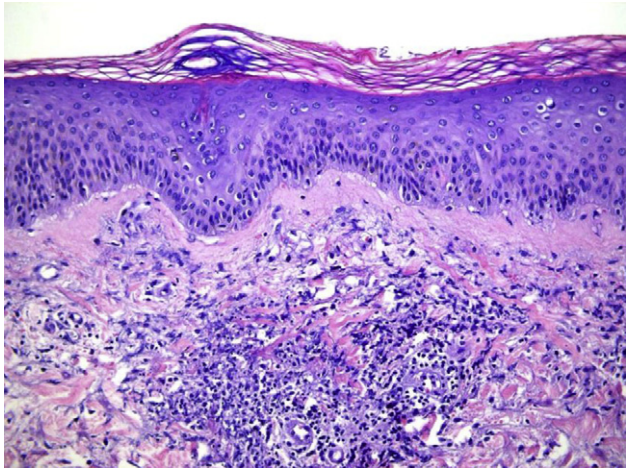

Fig. 2. Skin biopsy showed dense neutrophil infiltrate.

3. Discussion

The SS was described by Robert Douglas Sweet in 1964, typical manifestations are cutaneous lesion and clinical symptoms improve after treatment with systemic steroids. Extra cutaneous symptoms associated with SS are commons, occurs in ±40% of clinical presentations. Fever, arthritis, musculoskeletal and ocular involvements such as conjunctivitis, uveitis, episcleritis have been reported frequently in literature.[1,2]

Pulmonary involvement is very rare, in our review of 34 cases, the ratio man: female was 1:1, the age average is 57 years − old (±14 years old, range 25–82 years old). In 18 cases hematological disorders such as myelodisplastic syndrome, myeloproliferative disorder, agnogenic myeloid metaplasia, refractory anemia with excess blasts and idiopathic thrombocytopenia were present. Eight cases of SS with pulmonary involvement were in previously healthy people.[9,10,12,14,16,17,23,27] Summary of demographic, clinical, diagnosis, treatment and outcome of cases reported in literature are shown in Table 1.[2–30]

Skin involvement was the first manifestation in 16 of 34 cases. Typical symptoms are erythematous plaques and nodules, which may be recurrent and painful. Typical skin biopsy showed a dense infiltrate of neutrophils, primarily in dermis, associated to edema without vasculitis. In 12 of 34 cases, skins lesions and pulmonary involvements are simultaneous. If there is pulmonary involvement, it usually manifests with dry cough and dyspnea.[11]

Chest X-ray may reveal diffuse pulmonary infiltrated or pleural effusion, chest-CT usually confirms pulmonary involvement. Videobronchoscopy usually is normal. Bronchoalveolar lavage reveals high neutrophil (>50%) without organism in 14 cases. We did not find data of bronchoalveolar lavage in 20 cases, specially, cases reported before 1996.[2–7,9–14] Transbronchial biopsy frequently shows intraalveolar dense infiltration by neutrophils, similar to skin biopsies. In 15 of 24 cases, lung biopsies revealed interstitial inflammation, edema and alveolar infiltration by large number of neutrophils. In 10 cases the diagnosis was performed without biopsy, and in 9 cases by skin biopsy only.[3,9,13,19,25–28,30]

Systemic corticosteroid therapy is the treatment of choice for SS with pulmonary involvement, high doses of oral or intravenous

Table 1
Cases of SS with pulmonary improvement.

Reference	Year	Sex	Age	Comorbidities	Presentation	Bal	Radiology	Biopsy	Treatment	Outcome
Soderstrom RM	1981	F	50	AML	S → P	ND	Unilateral infiltrate + effusion		S	I
Gibson LE	1985	F	66	AMM	S → P	ND	Bilateral infiltrate	Extensive PMN infiltrate	S	I
Rodriguez de la Serna A	1985	F	68	Dressler's Syndrome	B	ND	Unilateral infiltrate + effusion		S+ Dapsone	I
Lazarus AA	1986	M	60	AML	B	ND	Unilateral infiltrate	Chronic intertitial pneumonitis + neutrophilic infiltrate	S	I
Keefe M	1988	F	67	PP	B	ND	Unilateral infiltrate		S	I
Hatch ME	1989	M	45	CML	S → P	ND	Bilateral infiltrate	Extensive PMN infiltrate + pleural and perivascular fibrosis	S	I
Cohen PR	1989	F	61	CML	B	ND	Bilateral infiltrate		S	I
Bourke SJ	1991	F	72	None	S → P	91% neutrophils	Bilateral infiltrate	Instertitial infiltrate + neutrophilic infiltrate	S	I
Takimoto CH	1991	F	54	MDS	B	ND	Unilateral infiltrate	Instertitial infiltrate + neutrophilic infiltrate	S	D
Chien SM	1991	M	58	None	P → S	ND	Unilateral infiltrate	Extensive PMN infiltrate	S	I
Komiya I	1991	M	54	RAEB	B	ND	Bilateral infiltrate	Instertitial infiltrate + neutrophilic infiltrate	S	D
Fett DL	1995	M	35	ITP	B	ND	Bilateral infiltrate + efussion		S	I
Fett DL	1995	M	46	DM	B	ND	Bilateral infiltrate + efussion	Mixed intertitial pneumonitis	S	I
Fett DL	1995	M	61	MPD	B	ND	Bilateral infiltrate		S	I
Fett DL	1995	F	74	RAEB	B	ND	Bilateral infiltrate + efussion		S	I
Reid PT	1996	M	34	None	P → S	ND	Unilateral infiltrate	Intertitial pneumonitis, cryptogenic organizing pneumonia	S	I
Rodot S	1996	F	63	AML	S → P	ND	Bilateral infiltrate		S	I
Thurnheer R	1997	F	62	None	S → P	78% neutrophils	Bilateral infiltrate	Neutrophilic infiltrate in skin biopsy	S	D
Peters FJP	1998	F	48	RAEB	P → S	ND	Unilateral infiltrate		S+ Chemo	I
Katsura H	1999	F	70	Sjogren	P → S	ND	Unilateral infiltrate	Intertitial pneumonitis	S	I
Alberts	2000	F	72	MDS	B	90% neutrophils	Bilateral infiltrate	Neutrophilic infiltrate in skin biopsy	S+ Chemo	I
Imanaga T	2000	M	55	None	S → P	Neutrophils	Bilateral infiltrate	Chronic intertitial infiltrate	S+ Cyclo	I
Longo MI et al	2001	M	51	None	S → P	Neutrophils	Unilateral infiltrate	Intertitial pneumonitis, cryptogenic organizing pneumonia	S	I
Astudillo L et al	2006	M	82	MDS	S → P	30% neutrophils	Interlobular septal thickening		S	I
Gard R et al	2006	F	25	MPD	B	Neutrophils	Unilateral infiltrate + effusion	Bronchiolitis obliterans organizing pneumonia	S+Dapsone	I
Petrig C	2006	M	67	CML	P → S	Neutrophils	Bilateral infiltrate	Neutrophilic infiltrate in skin biopsy	S	I
Fulton JC	2007	F	25	None	S → P	Neutrophils	Bilateral pulmonary nodules	Neutrophilic infiltrate in skin biopsy	S	I
Kushima H et al	2007	F	73	Previous SS	S → P	Neutrophils	Unilateral infiltrate	Chronic interstitial infiltrate with alveolar wall thickening and neutrophils	S	I
Aydemir	2008	M	32	CLD	S → P	60% neutrofilos	Bilateral infiltrate	Neutrophilic infiltrate in skin biopsy + vasculitis	S	I
Lawrence K	2008	M	54	Hypertention	P → S	ND	Unilateral infiltrate	Neutrophilic infiltrate in skin biopsy	S	I
Gaspar C	2008	F	76	IgA Myeloma	S → P	ND	ND	Neutrophilic infiltrate in skin biopsy	S	I
Robbins C et al	2009	F	26	None	S → P	Neutrophils	Intersticial + nodule	Airpace filling with agregated of neutrophils	S+ Colchicine	D
Aparicio V. et al	2010	M	67	Hypertention	S → P	Neutrophils	Unilateral infiltrate	Neutrophilic infiltrate in skin biopsy	S	D
Our case	2011	F	74	MDS	S → P	72% neutrophils	Unilateral infiltrate + effusion	Neutrophilic infiltrate in skin and lung biopsy	S	I

AMM: Agnogenic myeloid metaplasia; AML: Acute myeloid leukemia; B: Both; CML: Chronic myeloid leukemia; CLD: Chronic liver disease; Chemo: Chemotherapy; Cyclo: Cyclophospamide; D: Death; DM: Dermatomyositis; F: Female; I: Improvement; ITP: Idiopathic thrombocytopenia; M: Male; MDS: Myelodysplastic syndrome; MPD: Myeloproliferative disorder; PP: Plantar pustulosis; P → S: Skin after pulmonary; RAEB: Refractory anemia with excess blasts; S: Steroids; S → P: Pulmonary after skin.

corticosteroids decrease symptoms with prompt improvement. Immunosuppression with colchicine, cyclosporine and other drugs have been used for therapy. In our review, 32 cases were treated with prednisone; the combination with other immunosuppresor therapy was reported in 6 cases, typically with dapsone or colchicine.

The outcome of SS with pulmonary disease is good, only 5 patient's died (with ARDS) and 2 patient's had a recurrence of the disease. The most common outcome in SS with pulmonary disease is clinical and radiographic resolution.

Our patient presented an SS with pulmonary involvement with a medical history of myelodysplastic syndrome, an association

commonly seen. Poor response to antibiotic and clinical compromised was characteristic. BAL result and lung transbronchial biopsy revealed extensive neutrophil infiltrates. Prompt improvement of symptoms and pulmonary involvement with corticosteroid therapy in combination with skin and lung biopsies confirmed the diagnosis.

In conclusion, SS with pulmonary involvement is rare. Recognition of Sweet's Syndrome with lung involvement is important to prevent severe respiratory compromise.

Conflict of interest

None.

References

1. Sweet RD. An acute febril neutrophilic dermatosis. *Br J Dermatol* 1964;**76**:349–56.
2. Soderström RM. Sweet's Syndrome and acute myelogenous leukaemia: a case report and review of the literature. *Cutis* 1981;**28**:255–60.
3. Gibson LE, Dicken CH, Flach DB. Neutrophilic dermatoses and myeloproliferative disease: report of two cases. *Mayo Clin Proc* 1985;**60**:735–40.
4. Rodriguez de la Serna A, Domingo-Pedrol L, Blanch-Torra L. Acute febrile neutrophilic dermatosis (Sweet's Syndrome) associated with post-myocardial infarction syndrome (Dressler's syndrome). *Arch Intern Med* 1985;**145**:1522–4.
5. Lazarus AA, McMillan M, Miramadi A. Pulmonary involvement in Sweet's Syndrome (acute febrile neutrophilic dermatosis). Preleukemic and leukemic phases of acute myelogenous leukemia. *Chest* 1986 Dec;**90**(6):922–4.
6. Keefe M, Wakeel Ra, Kerr REI. Sweet's Syndrome, plantar pustulosis and vulval pustules. *Clin Exp Dermatol* 1988;**13**:344–6.
7. Hatch ME, Farber SS, Superfon NP, Ligorsky RD, Williams HE. Sweet's Syndrome associated with chronic myelogenous leukaemia. *J Am Osteopath Assoc* 1989;**89**:363–70.
8. Takimoto CH, Warnock M, Golden JA. Sweet's Syndrome with lung involvement. *Am Rev Respir Dis* 1991;**143**:177–9.
9. Chien SM, Jambrosic J, Mintz S. Pulmonary manifestations in Sweet's Syndrome: first report of a case with bronchiolitis obliterans organizing pneumonia. *Am J Med* 1991 Nov;**91**(5):553–4.
10. Bourke SJ, Quinn AG, Farr PM, Ashcroft T, Gibson GJ. Neutrophilic alveolitis in Sweet's Syndrome. *Thorax* 1992;**47**:572–3.
11. Fett DL, Gibson LE, Su WPD. Sweet's Syndrome: systemic signs and symptoms and associated disorders. *Mayo Clin Proc* 1995;**70**:234–40.
12. Rodot S, Lacour JP, Van Elslande L. Extracutaneous manifestations of neutrophilic dermatosis. *Ann Dermatol Venereol* 1996;**123**:129–34 [in French].
13. Thurnheer R, Stammberger U, Hailemariam S, Russi EW. Bronchial manifestation of acute neutrophilic dermatosis (Sweet's Syndrome). *Eur Respir J* 1998;**11**:978–80.
14. Reid PT, Alderdice J, Carson J, Sinnamon DG. Cryptogenic organizing pneumonia in association with Sweet's Syndrome. *Respir Med* 1996 Jan;**90**(1):57–9.
15. Alberts WA. 72-year-old man with fever, skin lesions, and consolidation on chest radiograph. *Chest* 2000;**118**:861–2.
16. Imanaga T, Hayashi T, Yoshii C, Suzuki S, Yatera K, Kido M. Pulmonary involvement in acute febrile neutrophilic dermatosis (Sweet's Syndrome). *Nihon Kokuyki Gakkai Zasshi* 2000;**38**:206–10 [in Japanese].
17. Longo MI, Pico M, Bueno C, Lazaro P, Serrano J, Lecona M. Sweet's Syndrome and bronchiolitis obliterans organizing pneumonia. *Am J Med* 2001;**111**:80–1.
18. Cohen PR, Kurzrock R. Sweet's Syndrome: a review of current treatment options. *Am J Clin Dermatol* 2002;**3**:117–31.
19. Petrig C, Bassetti S, Passweg J, Marsch S. Acute respiratory failure due to sweet syndrome. *Am J Med Sci* 2006 Mar;**331**(3):159–61.
20. Astudillo L, Sailler L, Launay F, Josse AG, Lamant L, Couret B, et al. Pulmonary involvement in Sweet's Syndrome: a case report and review of the literature. *Int J Dermatol* 2006 Jun;**45**(6):677–80.
21. Garg R, Soud Y, Lal R, Mehta N, Kone BC. Myelodysplastic syndrome manifesting as Sweet's Syndrome and bronchiolitis obliterative organizing pneumonia. *Am J Med* 2006 Nov;**119**(11):e5–7.
22. Komiya I, Tanoue K, Kakinuma K, Kaneda M, Shinohara T, Kuriya S. Superoxide anion hyperproduction by neutrophils in a case of myelodysplastic syndrome. Association of Sweet's Syndrome and interstitial pneumonia. *Cancer* 1991;**67**: 2337–41.
23. Kushima H, Mizunoe S, Ishii H, Hashinaga K, Yamasaki T, Kishi K, et al. A case of Sweet's syndrome with a variety of chest radiological findings. *Nihon Kokyuki Gakkai Zasshi* 2007 Sep;**45**(9):685–90 [Article in Japanese].
24. Katsura H, Motegi T, Yamada K, Uehara T, Gotoh R, Kida K, et al. Interstitial Pneumonitis Associated Sweet's Syndrome Elderly. *Nippon Ronen Igakkai Zasshi* 1999;**36**:887–92 [in Japanese].
25. Fulton JC. Rapidly progressive pulmonary sweet syndrome. *Chest* 2007. Case Reports 706S.
26. Lawrence K, Hachem R, Wildes TM, Canizares M. A 54-year-old man with a rash and pulmonary infiltrates. *Chest* 2008 Dec;**134**(6):1340–3.
27. Aydemir H, Oztoprak N, Celebi G, Altinyazar C, Barut F, Piskin N, et al. Pulmonary and central nervous system involvement in Sweet's Syndrome: a very rare case report. *Intern Med* 2008;**47**(16):1481–4.
28. Gaspar C, Leyral C, Orlandini V, Begueret H, Pellegrin JL, Doutre MS, et al. Lethal pulmonary involvement of neutrophilic dermatosis following erythropoietin therapy. *Ann Dermatol Venereol* 2008 May;**135**(5):384–8 [Article in French].
29. Robbins CM, Mason SE, Hughey LC. Sweet Syndrome with pulmonary involvement in a healthy young woman. *Arch Dermatol* 2009 Mar;**145**(3): 344–6.
30. Aparicio V, Gil P, Juárez A, Suárez C. Fatal sweet with pulmonary involvement. *Rev Clin Esp* 2010 Feb;**210**(2):96–7.